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=> d l19 1-12 bib abs

L19 ANSWER 1 OF 12 CA COPYRIGHT 2002 ACS
AN 132:31744 CA
TI Gene probes used for genetic profiling in healthcare screening and planning
IN Roberts, Gareth Wyn
PA Genostic Pharma Ltd., UK
SO PCT Int. Appl., 745 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9964627	A2	19991216	WO 1999-GB1780	19990604 <--

PI WO 9964627 A2 19991216
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRAI	GB 1998-12099	A	19980606
	GB 1998-13291	A	19980620
	GB 1998-13611	A	19980624
	GB 1998-13835	A	19980627
	GB 1998-14110	A	19980701
	GB 1998-14580	A	19980707
	GB 1998-15438	A	19980716
	GB 1998-15574	A	19980718
	GB 1998-15576	A	19980718
	GB 1998-16085	A	19980724
	GB 1998-16086	A	19980724
	GB 1998-16921	A	19980805
	GB 1998-17097	A	19980807
	GB 1998-17200	A	19980808
	GB 1998-17632	A	19980814
	GB 1998-17943	A	19980819

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies which comprises of the identification of the core group of genes and their sequence variants required to provide a broad base of clin. prognostic information - "genostics". The "Genostic.RTM." profiling of patients and persons will radically enhance the ability of clinicians, healthcare

professionals and other parties to plan and manage healthcare provision and the targeting of appropriate healthcare resources to those deemed most in need. The use of this invention could also lead to a host of new applications for such profiling technologies, such as identification of persons with particular work or environment related risk, selection of applicants for employment, training or specific opportunities or for the enhancing of the planning and organization of health services, education services and social services.

L19 ANSWER 2 OF 12 CA COPYRIGHT 2002 ACS
AN 132:31743 CA
TI Gene probes used for genetic profiling in healthcare screening and planning
IN Roberts, Gareth Wyn
PA Genostic Pharma Limited, UK
SO PCT Int. Appl., 149 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9964626	A2	19991216	WO 1999-GB1779	19990604 <--
	W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
	AU 9941586	A1	19991230	AU 1999-41586	19990604 <--
	AU 9941587	A1	19991230	AU 1999-41587	19990604 <--
	GB 2339200	A1	20000119	GB 1999-12914	19990604 <--
	GB 2339200	B2	20010912		
	EP 1084273	A1	20010321	EP 1999-925207	19990604
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
PRAI	GB 1998-12098	A	19980606		
	GB 1998-28289	A	19981223		
	GB 1998-16086	A	19980724		
	GB 1998-16921	A	19980805		
	GB 1998-17097	A	19980807		
	GB 1998-17200	A	19980808		
	GB 1998-17632	A	19980814		
	GB 1998-17943	A	19980819		
	WO 1999-GB1779	W	19990604		

AB There is considerable evidence that significant factor underlying the individual variability in response to disease, therapy and prognosis lies in a person's genetic make-up. There have been numerous examples relating that polymorphisms within a given gene can alter the functionality of the protein encoded by that gene thus leading to a variable physiol. response. In order to bring about the integration of genomics into medical practice and enable design and building of a technol. platform which will enable the everyday practice of mol. medicine a way must be invented for the DNA sequence data to be aligned with the identification of genes central to the induction, development, progression and outcome of disease or physiol. states of interest. According to the invention, the no. of genes and their configurations (mutations and polymorphisms) needed to be identified in order to provide crit. clin. information concerning individual prognosis is considerably less than the 100,000 thought to comprise the

human genome. The identification of the identity of the core group of genes enables the invention of a design for genetic profiling technologies.

L19 ANSWER 3 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:212403 BIOSIS
DN PREV199900212403
TI Differential sensitivity of transcription factors to mustard-damaged DNA.
AU Chen, Xin-Ming; Gray, Peter J.; Cullinane, Carleen; Phillips, Don R. (1)
CS (1) Department of Biochemistry, La Trobe University, Bundoora, Victoria, 3083 Australia
SO Chemico-Biological Interactions, (**March 1, 1999**) Vol. 118, No. 1, pp. 51-67.
ISSN: 0009-2797.
DT Article
LA English
SL English
AB Nitrogen mustard (bis(2-chloroethyl) methylamine, HN2) **inhibited** the binding of upstream factors Sp1 and AP2 to their consensus sequences. At concentrations where 50% of the consensus sequence DNA contained at least one lesion, HN2 **inhibited** formation of the Sp1 complex by 37% (40 muM HN2) and the AP2 complex by 40% (50 muM HN2). The binding of the TATA binding protein (TBP) to the TATA element was also **inhibited** by HN2, whereas sulphur mustard and the monofunctional sulphur mustard 2-chloroethyl ethyl sulphide (CEES) resulted in a disproportional extent of **inhibition** with respect to the level of alkylation. The level of alkylation of the TBP **oligonucleotide** varied significantly at 100 muM drug, with 80, 42 and 15% of HN2, sulphur mustard and CEES, respectively. However, this level of alkylation **inhibited** formation of the TBP-DNA complex by 70, 70 and 45% respectively. This differential sensitivity of transcription factors to mustard-induced DNA damage therefore appears to reside dominantly in the stereochemical differences between the specific mustard lesions.

L19 ANSWER 4 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 1
AN 1998:485001 BIOSIS
DN PREV199800485001
TI Quercetin **inhibits** hydrogen peroxide (H2O2)-induced NF-kappaB **DNA binding** activity and **DNA damage** in HepG2 cells.
AU Musonda, Clement A.; Chipman, James K. (1)
CS (1) Sch. Biochem., Univ. Birmingham, Edgbaston, Birmingham B15 2TT UK
SO Carcinogenesis (Oxford), (**Sept., 1998**) Vol. 19, No. 9, pp. 1583-1589.
ISSN: 0143-3334.
DT Article
LA English
AB We have investigated the effect of the plant-derived flavonoid quercetin in relation to potential oxidant and antioxidant activity on nuclear factor kappaB (NF-kappaB) binding activity and DNA integrity in HepG2 cells. Gel mobility shift assays using a gamma-32P-labelled NF-kappaB **oligonucleotide** probe showed that treatment of HepG2 cells with quercetin (up to 10 muM, sub-cytotoxic) did not elevate NF-kappaB binding activity of nuclear extract protein but did **inhibit** binding activity of an extract from cells treated with the oxidant H2O2. A similar **inhibition** by quercetin of H2O2-induced NF-kappaB transcriptional activation was demonstrated using a cat reporter gene assay. Considering oxidative DNA damage, using single cell gel electrophoresis (comet) assay we have demonstrated that quercetin (10 muM and below) did not induce DNA strand breaks. However, a marked and statistically significant ($P < 0.01$ at 10 muM) **inhibition** of strand breakage produced by H2O2 was

detected. The specific formation of 8-oxo-2'-deoxyguanosine (8-oxodG) in calf thymus DNA exposed to either gamma-irradiation or the Fenton reaction system was also **inhibited** (P < 0.01 at 10 muM) by quercetin in a dose-dependent manner. This was not accompanied by formation of 8-oxodG by quercetin itself. The **inhibition** of 8-oxodG formation by gamma-irradiation was more potent (IC50 = 0.05 muM) than that by the Fenton reaction (IC50 = 0.5 muM), implying that the mechanism of protection may be different between the two systems. The **inhibition** of both NF-kappaB **binding** activity and oxidative **DNA damage** suggests that its antioxidant potential outweighs its oxidative potential in a cellular environment, which may contribute to anticarcinogenic and antiinflammatory effects.

L19 ANSWER 5 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 2
AN 1996:375905 BIOSIS
DN PREV199699098261
TI A serine-kinase associated with the **p127**-l(2)gl tumour suppressor of Drosophila may regulate the binding of **p127** to nonmuscle myosin II heavy chain and the attachment of **p127** to the plasma membrane.
AU Kalmes, Andreas; Merdes, Gunter; Neumann, Beate; Strand, Dennis (1); Mechler, Bernard M.
CS (1) Dep. Dev. Genet., Deutsches Krebsforchungszentrum, Im Neuenheimer Feld 280, D-69120 Heidelberg Germany
SO Journal of Cell Science, (1996) Vol. 109, No. 6, pp. 1359-1368. ISSN: 0021-9533.
DT Article
LA English
AB The **p127** tumour suppressor protein encoded by the lethal(2)giant larvae, (l(2)gl), gene of Drosophila melanogaster is a component of a cytoskeletal network distributed in both the cytoplasm and on the inner face of the plasma membrane. The **p127** protein forms high molecular mass complexes consisting mainly of homo-**oligomerized** **p127** molecules and at least ten additional proteins. One of these proteins has been recently identified as nonmuscle myosin type II heavy chain. To determine the functional interactions between **p127** and other proteins present in the **p127** complexes, we analyzed **p127** for posttranslational modifications and found that **p127** can be phosphorylated at serine residues. In this report we describe the characteristics of a serine kinase which is associated with **p127**, as judged by its recovery in **p127** complexes purified by either gel filtration or immuno-affinity chromatography. This kinase phosphorylates **p127** in vitro and its activation by supplementing ATP results in the release of **p127** from the plasma membrane. Moreover, similar activation of the kinase present in immuno-purified **p127** complexes dissociates nonmuscle myosin II from **p127** without affecting the homo-**oligomerization** of **p127**. This dissociation can be **inhibited** by staurosporine and a 26mer peptide covering amino acid positions 651 to 676 of **p127** and containing five serine residues which are evolutionarily conserved from Drosophila to humans. These results indicate that a serine-kinase tightly associated with **p127** regulates **p127** binding with components of the cytoskeleton present in both the cytoplasm and on the plasma membrane.

L19 ANSWER 6 OF 12 ' MEDLINE
AN 94261648 MEDLINE
DN 94261648 PubMed ID: 8202546
TI Cisplatin-DNA adducts are molecular decoys for the ribosomal RNA transcription factor hUBF (human upstream binding factor).
AU Treiber D K; Zhai X; Jantzen H M; Essigmann J M

CS Department of Chemistry, Massachusetts Institute of Technology, Cambridge 02139.
NC CA52127 (NCI)
ES07020 (NIEHS)
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, **(1994 Jun 7)** 91 (12) 5672-6.
Journal code: PV3; 7505876. ISSN: 0027-8424.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199407
ED Entered STN: 19940714
Last Updated on STN: 19940714
Entered Medline: 19940706
AB The toxicity of DNA-damaging agents is widely believed to result from the formation of lesions that block polymerases or disrupt the integrity of the genome. A mechanism heretofore not addressed is that **DNA damage** may titrate essential **DNA-binding** proteins away from their natural sites of action. This report shows that the ribosomal RNA (rRNA) transcription factor hUBF (human upstream binding factor) binds with striking affinity (Kd(app) approximately 60 pM) to the intrastrand cis-[Pt(NH3)2](2+-d(GpG) crosslink formed by the anticancer drug cis-diamminedichloroplatinum(II) (cisplatin). When protein blots of human cell extracts are probed with cisplatin-modified DNA, 97- and 94-kDa proteins are detected, consistent with the known sites of hUBF species. A similar analysis of blots containing in vitro translated hUBF confirmed that the protein binds cisplatin adducts with high specificity. By contrast, DNA adducts of the clinically ineffective trans isomer of cisplatin, trans-diamminedichloroplatinum(II), are not recognized by hUBF. DNase I **inhibition** patterns of hUBF bound to a 100-base-pair DNA fragment containing a centrally located cis-[Pt(NH3)2](2+)-d(GpG) crosslink reveal specific protein-DNA interactions in a 14-base-pair region flanking the adduct. The affinity of hUBF for the rRNA promoter is similar (Kd(app) approximately 18 pM) to that measured for the cisplatin adduct. In addition, we observe that the hUBF-promoter interaction is highly sensitive to the antagonistic effects of cisplatin-DNA adducts. These results suggest that a cisplatin-mediated transcription-factor-hijacking mechanisms could disrupt rRNA synthesis, which is stimulated in proliferating cells.

L19 ANSWER 7 OF 12 MEDLINE
AN 93252924 MEDLINE
DN 93252924 PubMed ID: 8387518
TI The DNA helicase activities of Rad3 protein of Saccharomyces cerevisiae and helicase II of Escherichia coli are differentially **inhibited** by covalent and noncovalent DNA modifications.
AU Naegeli H; Modrich P; Friedberg E C
CS Department of Pathology, University of Texas Southwestern Medical Center, Dallas 75235-9072.
NC CA12428 (NCI)
GM23719 (NIGMS)
SO JOURNAL OF BIOLOGICAL CHEMISTRY, **(1993 May 15)** 268 (14) 10386-92.
Journal code: HIV; 2985121R. ISSN: 0021-9258.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199306
ED Entered STN: 19930618
Last Updated on STN: 19970203

Entered Medline: 19930608

AB Rad3 protein of Saccharomyces cerevisiae is a DNA-dependent ATPase that acts as a DNA helicase on partially duplex substrates. Rad3 **protein** is required for **damage-specific** incision of **DNA** during the nucleotide excision repair (NER) pathway in yeast. Helicase II of Escherichia coli is also a DNA helicase, but it is involved in postincision events in NER. Previous investigations have demonstrated that the DNA helicase activities of Rad3 protein and helicase II are both **inhibited** by DNA damage. In the present study we have compared the response of yeast Rad3 protein and E. coli helicase II to a broad spectrum of DNA modifications. The Rad3 helicase activity is considerably more sensitive to ultraviolet radiation damage and cisplatin adducts in DNA than to drugs that interact noncovalently with duplex DNA. Conversely, E. coli helicase II is highly sensitive to noncovalent DNA modifications but less sensitive than Rad3 protein to ultraviolet radiation damage or cisplatin adducts. We also show that Rad3 protein and helicase II differ in their ability to form stable protein-DNA complexes at sites of DNA damage. Hence, DNA helicases that catalyze distinct steps in NER respond differently to chemical and conformational states of the DNA substrate. The observation that Rad3 protein is particularly sensitive to covalent but not noncovalent alterations in DNA structure is consistent with the hypothesis that this enzyme may have adopted a highly specialized role in damage-specific recognition during NER.

L19 ANSWER 8 OF 12 CA COPYRIGHT 2002 ACS

AN 119:111441 CA

TI Phosphorylation and nucleotide-dependent dephosphorylation of hepatic polypeptides related to the plasma cell differentiation antigen PC-1

AU Uriarte, Matxalen; Stalmans, Willy; Hickman, Scot; Bollen, Mathieu

CS Fak. Geneeskunde, Kathol. Univ. Leuven, Louvain, B-3000, Belg.

SO Biochem. J. (**1993**), 293(1), 93-100
CODEN: BIJOAK; ISSN: 0306-3275

DT Journal

LA English

AB A glycoprotein fraction was isolated from rat liver membranes by affinity chromatog. on immobilized wheat-germ lectin. Incubation of this fraction with MgATP or MgGTP resulted in a sequential phosphorylation and dephosphorylation of a complex of 3 polypeptides (118, 128 and 197 kDa on SDS/PAGE) with N-linked sialyloligosaccharides. Each polypeptide was recognized by polyclonal antibodies against recombinant plasma cell differentiation antigen PC-1. The relationship of the 118 kDa and 128 kDa polypeptides with PC-1 was confirmed by observations that they are linked by disulfide bonds into a larger protein, and that they are exclusively phosphorylated on Thr residues. Phosphorylation of p118, **p128** and p197 only occurred after a lag period (up to 90 min at 30 .degree.C), which lasted until most of the ATP had been converted to adenosine and Pi, with ADP and AMP as intermediate products. The length of the latency period increased with the concn. of initially added ATP (5-1000 .mu.M) and could be prolonged by a second addn. of similar concns. of ATP, ADP, AMP and various nucleotide analogs. Most potent were the .alpha..beta.-methylene derivs. of ADP and ATP. Adenosine was poorly effective. AMP, ADP, and perhaps ATP, emerge as the direct determinants of the latency. After further purifn. of the lectin-purified membrane fraction on anion-exchange and mol.-sieve columns, the complex of p118, **p128** and p197 was still capable of autophosphorylation and dephosphorylation. The dephosphorylation was not affected by classical **inhibitors** (NaF, okadaic acid, EDTA, EGTA, phenylalanine). It was stimulated by about 20-fold by various adenine nucleotides and analogs, with the same order of efficiency as noted for the induction of the latency. A similar stimulation of dephosphorylation was caused by 0.5 mM Ns3VO4, which also prevented the phosphorylation of the 3 polypeptides. The likely

explanation for the latency that precedes the phosphorylation of the membrane proteins is that the action of a protein kinase is initially offset by nucleotide-stimulated dephosphorylation.

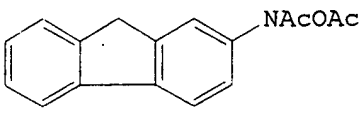
L19 ANSWER 9 OF 12 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.DUPLICATE 3
AN 1992:95047 BIOSIS
DN BA93:51597
TI THE DNA HELICASE AND ADENOSINE TRIPHOSPHATASE ACTIVITIES OF YEAST RAD3 PROTEIN ARE **INHIBITED** BY DNA DAMAGE A POTENTIAL MECHANISM FOR DAMAGE-SPECIFIC RECOGNITION.
AU NAEGELI H; BARDWELL L; FRIEDBERG E C
CS LAB. MOL. PATHOL., DEP. PATHOL., UNIV. TEXAS SOUTHWESTERN MED. CENTER DALLAS, DALLAS, TEXAS 75235.
SO J BIOL CHEM, (1992) 267 (1), 392-398.
CODEN: JBCHA3. ISSN: 0021-9258.
FS BA; OLD
LA English
AB Purified Rad3 protein from the yeast Saccharomyces cerevisiae is a single-stranded DNA-dependent ATP-ase and also acts as a DNA helicase on partially duplex DNA. In this study we show that the DNA helicase activity is **inhibited** when a partially duplex circular DNA substrate is exposed to ultraviolet (UV) radiation. **Inhibition** of DNA helicase activity is sensitive to the particular strand of the duplex reigon which carrier the damage. **Inhibition** is retained if the single-stranded circle is irradiated prior to annealing to an unirradiated **oligonucleotide**, but not if a UV-irradiated **oligonucleotide** is annealed to unirradiated circular single-stranded DNA. UV irradiation of single-stranded DNA or deoxyribonucleotide homopolymers also **inhibits** the ability of these polynucleotides to support the hydrolysis of ATP by Rad3 protein. UV radiation damage apparently blocks translocation of Rad3 protein and results in the formation of stable Rad3 protein-UV-irradiated DNA complexes. As a consequence, Rad3 protein remains sequestered on DNA, presumably at sites of base damage. The sensitivity of Rad3 protein to the presence of DNA damage on the strand along which it translocates provides a potential mechanism for damage recognition during nucleotide excision repair and may explain the absolute requirement for Rad3 **protein** for **damage-specific** incision of **DNA** in yeast.

L19 ANSWER 10 OF 12 CA COPYRIGHT 2002 ACS
AN 113:221 CA
TI Characterization of a DNA damage-recognition protein from mammalian cells that binds specifically to intrastrand d(GpG) and d(ApG) DNA adducts of the anticancer drug cisplatin
AU Donahue, Brian A.; Augot, Marianne; Bellon, Steven F.; Treiber, Daniel K.; Toney, Jeffrey H.; Lippard, Stephen J.; Essigmann, John M.
CS Whitaker Coll. Health Sci. Technol., Massachusetts Inst. Technol., Cambridge, MA, 02139, USA
SO Biochemistry (**1990**), 29(24), 5872-80
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB A factor was identified in exts. from human HeLa and hamster V79 cells that retards the electrophoretic mobility of several DNA restriction fragments modified with the antitumor drug cis-diamminedichloroplatinum(II) (cisplatin). Binding of the factor to cisplatin-modified DNA was sensitive to pretreatment with proteinase K, establishing that the factor is a protein. Gel mobility shifts were obsd. with probes contg. as few as seven Pt atoms per kilobase of duplex DNA. By competition expts. the dissocn. const., Kd, of the protein from

cisplatin-modified DNA was estd. to be (1-20) .times. 10-10 M. Protein binding is selective for DNA modified with cisplatin, [Pt(en)Cl2] (en, ethylenediamine), and [Pt(dach)Cl2] (dach, 1,2-diaminocyclohexane) but not with chemotherapeutically inactive trans-diamminedichloroplatinum(II) or monofunctionally coordinating [Pt(dien)Cl]Cl (dien, diethylenetriamine) complexes. The protein also does not bind to DNA contg. UV-induced photoproducts. The protein binds specifically to 1,2-intrastrand d(GpG) and d(ApG) cross-links formed by cisplatin, as detd. by gel mobility shifts with synthetic 110-bp duplex **oligonucleotides**; these modified **oligomers** contained five equally spaced adducts of either cis-[Pt(NH3)2d(GpG)] or cis-[Pt(NH3)2d(ApG)]. **Oligonucleotides** contg. the specific adducts cis-[Pt(NH3)2d(GpTpG)], trans-[Pt(NH3)2d(GpTpG)], or cis-[Pt(NH3)2(N3-cytosine)d(G)] were not recognized by the protein. The apparent mol. wt. of the protein is 91,000, as detd. by sucrose gradient centrifugation of a prepn. partially purified by ammonium sulfate fractionation. Binding of the protein to platinum-modified DNA does not require cofactors but is sensitive to treatment with 5 mM MnCl2, CdCl2, CoCl2, or ZnCl2 and with 1 mM HgCl2. This protein, alone or in conjunction with other cellular constituents, could be of general importance in the initial stages of processing of mammalian DNA damaged by cisplatin or other genotoxic agents and may belong to a wider class of such cellular damage-recognition proteins.

L19 ANSWER 11 OF 12 CA COPYRIGHT 2002 ACS
AN 113:17620 CA
TI NMR studies of the interaction of bleomycin with (dC-dG)3
AU Gamcsik, Michael P.; Glickson, Jerry D.; Zon, Gerald
CS Sch. Med., Johns Hopkins Univ., Baltimore, MD, 21205, USA
SO J. Biomol. Struct. Dyn. (**1990**), 7(5), 1117-33
CODEN: JBSDD6; ISSN: 0739-1102
DT Journal
LA English
AB The interaction of bleomycin A2 and Zn(II)-bleomycin A2 with the **oligonucleotide** (dC-dG)3 has been monitored by NMR spectroscopy. Binding of the drug to the **oligonucleotide** is indicated by an upfield shift of the bithiazole proton resonances consistent with partial intercalation of this group between base pairs. The effect of temp. and ionic strength on the binding of both free bleomycin and the Zn(II) complex has been studied. Consistent with earlier studies on polynucleotides, the rate of exchange between the free drug and the drug-**oligonucleotide** complex is rapid on the 1H NMR chem. shift time scale. Binding of the **oligonucleotide** induced changes in resonances assigned to protons in the metal-binding region of Zn(II)-bleomycin. Intermol. nuclear Overhauser effect enhancements between bleomycin and the **oligonucleotide** have not been detected.

L19 ANSWER 12 OF 12 CA COPYRIGHT 2002 ACS
AN 98:1478 CA
TI Mechanisms for the recognition of chemically-modified DNA by peptides and proteins
AU Helene, Claude; Toulme, Jean Jacques; Behmoaras, Tula; Cazenave, Christian
CS Lab. Biophys., Mus. Natl. Hist. Nat., Paris, 75005, Fr.
SO Biochimie (**1982**), 64(8-9), 697-705
CODEN: BICMBE; ISSN: 0300-9084
DT Journal
LA English
GI



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AB **Oligopeptides** contg. arom. and basic residues (such as Lys-Trp-Lys [38579-27-0]) and the single-strand binding protein coded for by gene 32 of bacteriophage T4 were used as probes for the structure of damaged sites in double-stranded DNA which has been chem. modified either by carcinogens such as aminofluorene derivs. and alkylating agents or by antitumor substances such as Pt derivs. The binding of the 2 probes to chem.-modified DNA was followed by fluorescence spectroscopy. Stacking interactions of the arom. residue of Lys-Trp-Lys are strongly favored in locally-denatured regions of DNA; they are characterized by a complete quenching of the tryptophan fluorescence. The gene 32 protein from phage T4 binds in a noncooperative way to single-stranded regions induced by chem. modification of DNA; this binding leads to a quenching of the protein fluorence. Modification of DNA by N-acetoxy-N-2-acetylaminofluorene (I) [6098-44-8] creates opened regions which are recognized by both Lys-Trp-Lys and the gene 32 protein. Three platinum derivs. were used to modify DNA: cis-Pt [15663-27-1], trans-Pt [14913-33-8] and Pt-dien [15522-23-3]. The 1st one exhibits an antitumor activity whereas the 2 others are inactive. Only cis-Pt creates strong binding sites in DNA for both the tripeptide Lys-Trp-Lys and the gene 32 protein. Methylation of guanine (N7) and adenine (N3) by Me2SO4 does not affect the binding of either probe. Removal of the methylated purines without cleavage of the phosphodiester backbone creates apurinic sites which are selectively recognized by the tripeptide Lys-Trp-Lys; the assocn. const. is >2 orders of magnitude higher than for native DNA. In contrast, the gene 32 protein does not bind more to apurinic than to native sites. **Oligopeptides** contg. lysyl and tryptophanyl (or tyrosyl) residues are shown to cleave phosphodiester bonds at apurinic sites upon incubation of the complexes at 37.degree.. These **oligopeptides** therefore mimic apurinic endonuclease [61811-29-8]; they make use of their arom. residue to anchor at apurinic sites and of their lysyl amino groups to cleave the phosphodiester bond through a .beta. elimination reaction. Cleavage of the phosphodiester bond at apurinic sites reduces the affinity of the tripeptide; on the contrary the gene 32 protein exhibits a strong binding for these nicked apurinic sites. A model is proposed for the recognition of apurinic sites in DNA and for the sequential action of apurinic endonucleases and single-strand binding proteins in the repair of apurinic DNA. Preliminary expts. were carried out to characterize the binding of the recA gene product from Escherichia coli to single-stranded DNA; this binding induced an ATPase and a proteolytic activity of the recA protein. Fluorescence quenching is obsd. when the recA protein binds to polydT and single-stranded DNA. However, the apparent size of the binding site is quite different for these 2 ligands. These results are discussed with resp. to a possible base-sequence selectivity in the binding of recA protein to single strands and to the role of locally unpaired regions of chem.-damaged DNA in the activation of the proteolytic activity of the recA protein.

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(FILE 'HOME' ENTERED AT 15:17:35 ON 23 APR 2002)

FILE 'BIOSIS, MEDLINE, SCISEARCH, CA' ENTERED AT 15:17:44 ON 23 APR 2002
L1 1 S POPOFF, W?/AU
L2 112 S POPOFF, I?/AU

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                E L1
L3             12 S L2 AND ANTISENSE
L4           2533 S WYATT, J?/AU
L5             69 S L4 AND ANTISENSE
L6             22 S L5 AND PY<=2000
L7             11 DUP REMOVE L6 (11 DUPLICATES REMOVED)
L8            156 S P127 OR (DAMAGE!SPECIFIC DNA BINDING PROTEIN)
L9            139 S DAMAGE (N) SPECIFIC (3N) DNA (3N) PROTEIN
L10            24 S P128
L11           859 S DNA (5N) DAMAGE (5N) BINDING
L12             0 S L8, L9, L10, L11, AND (ANTISENSE OR OLIGO?)
L13            60 S L11 AND (ANTISENSE OR OLIGO?)
L14             8 S L8-L11 AND (ANTISENSE OR OLIGO)
L15             0 S (L8 AND L9 AND L10 AND L11) AND (ANTISENSE OR OLIGO?)
L16            82 S L8-L11 AND (ANTISENSE OR OLIGO?)
L17            73 S L16 AND PY<=2000
L18            21 S L17 AND INHIBIT?
L19            12 DUP REMOVE L18 (9 DUPLICATES REMOVED)

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